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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HURT, SHARON L	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/620,787	SIMARD ET AL.	
	Examiner	Art Unit	
	Sharon Hurt	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _____ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-17 and 20-29* is/are pending in the application.

4a) Of the above claim(s) *3-6 and 12-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7-11 and 20-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *July 17, 2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 26, 2007 has been entered.

Response to Amendment

The amendments to the claims filed January 26, 2007 has been entered. Claim 29 is newly added. Claims 18-19 have been cancelled.

Status of the Claims

Claims 1-17 and 20-29 are pending. Claims 3-6 and 12-17 have been withdrawn. Claims 1-2, 7-11 and 20-29 are under examination on the merits.

Response to Arguments

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1-2, 7-11 and 20 under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. and Thomson et al. **is maintained**. Applicant's arguments filed January 26, 2007 have been fully considered but they are not persuasive. Applicant argues that Hooper does not teach nor suggest polyproteins or immunogenic compositions comprised of polyproteins. Hooper teaches that the immunogen can be administered with adjuvants or as a fusion protein to induce an immune response and that fusion proteins comprise the peptide against which an immune response is desired coupled to carrier proteins (page 3, paragraph 022). Applicant's specification defines "polyprotein" as "more than one protein, or polypeptide, made as a result of a single transcriptional event that has not been cleaved into individual protein or polypeptide chains" (page 7, paragraph 027). Hooper teaches about fusion proteins, which are polyproteins therefore, Hooper teaches polyproteins.

Applicant also argues that Thomson does not teach or suggest polyproteins, particularly comprising more than mere epitope sequences. Thomson teaches about a "polyepitope" or "polytope" protein, which is defines as more than one peptide, which is made as a result of a single event and not cleaved (page 1717). Therefore Thomson's polyepitope meets the definition of a polyprotein in the instant invention as set forth supra. Applicant further argues that Thomson does not disclose vaccines for smallpox. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that the combination of Hooper and Thomson do not render the pending claims obvious because they do not teach or suggest a polyprotein combining multiple proteins having sequences longer that epitopes. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., sequences longer than epitopes) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that there is no expectation of success to combine the teachings for generating neutralizing antibodies to vaccinia-associated proteins with teachings of epitope-based CTL vaccines to yield polyprotein-based immunogenic compositions vaccines for poxviruses. Hooper teaches that there are several drawbacks with vaccinia immune globulin to treat disease because it is mode from human volunteers and could cause infectious lesions or scaring (page 1, paragraph 003). Therefore, there is a need for a safe and effective immune glogulin composition which does not rely on human donors (page 1, paragraph 004). Applicant's also argues that the combination of Hooper and Thomson would not suggest to one of ordinary skill in the art that a polyprotein comprising external immunogens or complete proteins of membrane-associated proteins of variola major or immunologically cross-reactive poxviruses would have a reasonable expectation of success. Hooper teaches that the vaccinia immunoglobulin composition which is composed of one or more monoclonal antibodies against vaccinia antigens is important for protection (page 1, paragraph 005).

The rejection of claim 21 under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. in view of Thomson et al. as applied to claims 1-2, 7-11 and 20 above, and further in view of Curiel et al. **is maintained**. Applicant's arguments have been fully considered but they are not persuasive. Applicant argues that the combination of Hooper, Thomson and Curiel do not teach or suggest all of the elements of claim 21. The arguments over Hooper and Thomson have been addressed *supra*. Curiel teaches binding with a biotin-streptavidin bridge therefore, the combined teachings of Hooper, Thomson and Curiel teach the elements of the instant claimed invention.

The rejection of claim 22 under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. in view of Thomson et al. as applied to claims 1-2, 7-11 and 20 above, and further in view of Rutter et al. **is maintained**. Applicant's arguments have been fully considered but they are not persuasive. Applicant argues that the deficiencies of Hooper and Thomson are not remedied by Rutter. Applicant also argues that the combination of Hooper, Thomson and Rutter do not teach or suggest all the elements of claim 22. The arguments over Hooper and Thomson have been addressed *supra*. Rutter teaches about administering a nucleic acid vaccine which comprises an agent to facilitate delivery of the vaccine, wherein the agent is a polypeptide, liposome, etc. Since there are no deficiencies in Hooper and Thomson, the combined teachings including Rutter teaches the limitation of claim 22.

The rejection of claims 23-26 under 35 U.S.C. 103(a) as being unpatentable over Hooper et al. in view of Thomson et al. as applied to claims 1-2, 7-11 and 20 above, and further in view

of Newton et al. **is maintained** for claims 23-26, newer claims **27-28** and newly added claim **29**. Applicant's arguments have been fully considered but they are not persuasive. Applicant argues that the deficiencies of Hooper and Thomson are not remedied by Newton. Applicant also argues that the combination of Hooper, Thomson and Newton do not teach or suggest all the elements of claim 23. The arguments over Hooper and Thomson have been addressed *supra*. Newton teaches about flexible peptide linkers used to join fusion proteins and attaching a poly-histidine affinity tag to facilitate purification of the fusion proteins. Since there are no deficiencies in Hooper and Thomson, the combined teachings including Newton teaches the limitation of claim 23.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of

Patent Applications Under the 35 U.S.C. 112, & 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117). A review of the language of the claim indicates that these claims are drawn to a genus, i.e. **consensus sequence**.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1),

the court states An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.

There is a single species of the claimed genus disclosed that is within the scope of the claimed genus, *i.e.* a variola nucleic acid sequence. The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claim encompasses numerous species that are not further described. There is substantial variability among the species. In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is a variola consensus sequence. One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus. The specification does not clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed (see *Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

The skilled artisan cannot envision the detailed structure of a genus of compounds that are contemplated in the invention. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The first paragraph of 35 U.S.C. 112 states: "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring ingenuity beyond that to be expected of one of ordinary skill in the art (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)). The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the

relative skill of those In the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The instant disclosure fails to meet the enablement requirement for the following reasons:

The nature of the invention: The claimed invention is drawn to a polyprotein comprising external immunogens of at least two membrane-associated proteins, wherein antibodies against one of the proteins are synergistic with antibodies against the at least one other protein.

The state of the prior art: The art teaches that certain antibody combination synergized in both neutralization rate and potency, combination that did not clearly synergize in potency could still significantly synergize in neutralization rate. The art also teaches that it is important to establish defined antibody cocktails for prophylactic and therapeutic purposes as described by Sanna et al. (Virology, May 2000, Vol. 270, No. 2, pages 386-396) (Abstract). The art also teaches the certain antibody combinations in dose-effective assays have synergism; however, it does not teach that all synergistic antibodies are neutralizing antibodies.

The amount of direction or guidance present and the presence or absence of working examples: Given the teachings of unpredictability in the art regarding the structural and functional differences in the synergism of antibodies, detailed teachings are required in the disclosure to enable the full scope of the claims. These teachings are absent. There are no working examples for synergism of antibodies.

The breadth of the claims and the quantity of experimentation needed: Because the invention encompasses proteins that are synergistic with antibodies and because the specification fails to provide guidance as to how to use the claimed method, it would require undue

experimentation by one of skill in the art to be able to practice the claimed invention commensurate in scope with the claims.

No claims allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon Hurt whose telephone number is 571-272-3334. The examiner can normally be reached on M-F 8:00 - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Hurt

March 30, 2007

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